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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/058,350 04/10/98 SIMMS

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HM22/0327
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EXAMINER

OWENS JR, H

ART UNIT

PAPER NUMBER

1623
DATE MAILED:

17-27
03/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No. 09/058,350	Applicant(s) Simms
Examiner Howard Owens	Group Art Unit 1623

Responsive to communication(s) filed on Nov 8, 2000

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 2-11 and 13-22 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

Claim(s) 2-11 and 13-22 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 15

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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Response to Arguments

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The following is in response to the amendment filed 1/16/01:

An action on the merits of claims 2-11 and 13-22 is contained herein below.

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The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

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35 U.S.C. § 103

Applicant's arguments filed 11/08/2000 have been fully considered but they are not persuasive.

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Claims 2-11, 13-22 and newly added 23-34 are rejected under 35 U.S.C. § 103 as being unpatentable over Sambrook et al. (*Molecular Cloning: A Laboratory Manual*, Second Edition; Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1989) in combination with Chomczynski (5,346,994) and newly cited Perlman, U.S. Patent No. 5,098,603.

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Claims 2 - 11 are directed to an RNA isolation reagent comprising at least one nonionic detergent (0.1 - 1.0%), a chelating agent (20 - 250 mM), a phenol (10%-60%), and a phenol stabilizer (15-55%).

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Claims 13-34 are directed to a RNA extraction reagent and a method for providing cytoplasmic RNA from a sample comprising mixing said sample with an RNA extraction reagent comprising at least one nonionic detergent, at least one phenol and at least one phenol solubilizer, adding a haloalkane to the mixture and precipitating cytoplasmic RNA.

Applicant asserts "that contrary to the Examiner's assertion, the specification at page 2 does not acknowledge that Sambrook discloses a method for isolating RNA that uses phenol." Although the instant specification does not state the use of phenol by

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Sambrook *et al.*, the use of a non-ionic detergent, RNase inhibitors and no chaotropic agent by Sambrook *et al.* is cited, p.2, line 13, of the instant specification, wherein it is stated "Sambrook(*supra*, at sections 7.6-7.9)discloses an alternative protocol for the isolation of cytoplasmic RNA extraction RNA from mammalian cells, which uses a non-disruptive RNA extraction reagent at physiological pH and salt concentration, instead of high concentrations of chaotropic salts. The extraction reagent contains an RNase inhibitor to protect the RNA during the isolation procedure and a nonionic detergent that solubilizes the cell membrane while leaving the nuclear membrane intact, to release cytoplasmic RNA." Thus the use of a nonionic detergent within the art of nucleic acid purification is not novel within the art of RNA extraction. Along with the use of the nonionic detergent, the use of phenol and a solubilizer is not novel as Sambrook *et al.* teaches the use of phenol, a haloalkane-chloroform and a solubilizer-isoamyl alcohol in the extraction of RNA (Appendix E.3 and B.5). Chomczynski was cited to further demonstrate the use of phenol and a solubilizer, particularly glycerol, in nucleic acid extraction. The use of a solubilizer with phenol is mutually exclusive of the presence of a chaotropic agent. The prior art of Sambrook and Chomczynski both demonstrate this as the former does not use a chaotropic agent and the latter does. Applicant seems to assert that one of skill in the art would not have a motivation to use a solubilizer with phenol based on the presence of other agents, even though the prior art teaches the use of phenol with a solubilizer in nucleic acid extractions wherein both chaotropic and non-chaotropic agents exist.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA

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1971). In the instant application, applicant has not set forth reagents which have not been used in combination in the art for the extraction of RNA, moreover, the prior art has set forth the motivation for the use of the reagents cited supra in extraction reagents of RNA.

5 Although the identical concentration ranges are not disclosed in the references cited supra, proportions of ingredients, to impart patentability to an otherwise obvious chemical composition, must produce more than a mere difference in degree in the properties of the composition. The proportions must be critical,i.e. they must produce a difference in kind rather than degree, which is not seen in the instant application.

10 With regard to the use of chelators within the instant claims, claims 23 and 29 are drawn to the use of chelators with the instant composition. As cited in the office action mailed 5-9-2000, the motivation to use a chelator within the instant composition is clearly set forth in Perlman as "Perlman teaches (col. 4, lines 37-51) the use of chelators such as EDTA when performing nucleic acid extractions with phenolic solutions to remove traces of divalent metal ions, some of which are known to catalyze the oxidation of phenol; moreover, Perlman further teaches that when even minute traces of metal ions are present, phenol solution is prone to catalytic oxidation." , which counters applicant's assertion in the instant specification on p. 4, line 26 that the use of chelators to protect nucleic acids is novel. Given that 8-hydroxyquinoline has long been regarded in this art as a chelator of divalent cations, one of skill in the art would have a reasonable expectation of success in the use of 8-hydroxyquinoline with phenol to reduce catalytic oxidation per the teachings of Perlman.

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Applicant's representative asserts that the DeBonville reference does not cure the deficiencies of Sambrook et al. or Chomczynski because "DeBonville et al is directed to methods of isolating DNA, not RNA. The DNA reagent composition contains, inter alia, phenol, isoamyl alcohol and 8-hydroxyquinoline. This composition does not contain the ingredients required to isolate RNA as set forth in the claimed reagents." If applicant's assertions are true, then the instant claims are also invalid with

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regard to the isolation of RNA given that these components are the same components applicant sets forth in claims 21 and 25, wherein phenol, a phenol solubilizer-exemplary of isoamyl alcohol, and 8-hydroxyquinoline are claimed.

For the reasons cited supra, the 35 U.S.C. 103 rejection of record is maintained .

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THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within 10 TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later 15 than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mr. Howard Owens whose telephone number is (703) 306-4538. The examiner can normally be reached on Tuesday-Friday 9 a.m.-6:30 p.m. (EST).

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If attempts to reach the examiner by telephone are unsuccessful, Mr. Gary Geist (703) 308-1701, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed 25 to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.



GARY GEIST
SUPERVISORY PATENT EXAMINER
TECH CENTER 1600